Psychiatric Briefs

With our first issue of *The Primary Care Companion*, we are introducing a feature called "Psychiatric Briefs." In a sense, this section is the very truest expression of our commitment to provide you, the primary care physician, with the information you may find helpful in making informed decisions about the care of your patients who suffer from psychiatric disorders. This feature will highlight abstracts from our sister publication, *The Journal of Clinical Psychiatry*, and in the future, it will include pertinent summaries from the general scientific literature. We hope you find this section clinically relevant to your practice and that it will encourage you to expand your horizons.

A Controlled, Prospective, 1-Year Trial of Citalopram in the Treatment of Panic Disorder

Lepola UM, Wade AG, Leinonen EV, et al.

Background: The objective of this study was to evaluate the efficacy and tolerability of citalopram in the long-term treatment of adult outpatients with panic disorder with or without agoraphobia. ***Method:*** Patients in this double-blind, parallel-group trial were assigned to 1 of 3 fixed dosage ranges of citalopram (10 or 15 mg/day, 20 or 30 mg/day, or 40 or 60 mg/day), 1 dosage range of clomipramine (60 or 90 mg/day), or placebo. After the completed 8-week acute treatment period, the eligible patients could continue the treatment for up to 1 year. Of the 475 patients who were randomly assigned for the short-term trial, 279 agreed to continue double-blind treatment at their assigned doses. The primary efficacy measure used was the Clinical Anxiety Scale panic attack item, and the response was defined as no panic attacks (score of 0 or 1). The other key measures used were the Physician's Global Improvement Scale, the Patient's Global Improvement Scale, and the Hamilton Rating Scale for Anxiety (HAM-A). ***Results:*** In all drug-treated groups, except the group receiving the lowest citalopram dose, the treatment outcome was generally better than with placebo. As determined by a life table analysis of response, the probability of response during the 12 months was significantly greater with all treatment regimens than with placebo ($p < .05$), with citalopram 20 or 30 mg/day demonstrating the best response. Panic attacks tended to disappear in all patients remaining in the study until the end of follow-up. Analysis of the difference in the number of patients in different treatment groups remaining in the study (perhaps the best measure of long-term efficacy) also demonstrated that the patients treated with citalopram in dosage ranges of 20 or 30 mg/day and 40 or 60 mg/day had better response than placebo-treated patients ($p < .0002$ and $p < .004$, respectively). HAM-A and Global Improvement Scale scores also showed that patients treated with active drug showed greater improvement than placebo-treated patients. All treatment groups showed no new or exceptional adverse event clusters. ***Conclusion:*** Citalopram in the dosage range of 20 to 60 mg/day is effective, well tolerated, and safe in the long-term treatment of patients who have panic disorder.

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The Treatment of Chronic Depression, Part 2: A Double-Blind, Randomized Trial of Sertraline and Imipramine

Keller MB, Gelenberg AJ, Hirschfeld RMA, et al.

Background: Chronic depression appears to be a common, frequently disabling illness that is often inadequately treated. Unlike for episodic depressions with shorter illness duration, neither acute nor long-term treatment approaches for chronic depression have been well studied. ***Method:*** 635 outpatients at 12 sites who met DSM-III-R criteria for chronic major depression or double depression were randomly assigned to 12 weeks of double-blind treatment with either sertraline (in daily doses of 50–200 mg) or imipramine (in daily doses of 50–300 mg). Efficacy and safety were assessed either weekly or every 2 weeks during the 12 weeks of acute treatment. ***Results:*** Despite high rates of chronicity (mean duration of major depression = 8.9 ± 9.1 years; mean duration of dysthymia = 23 ± 13 years) and high rates of comorbidity, 52% of patients achieved a satisfactory therapeutic response to sertraline or imipramine (by a conservative, intent-to-treat analysis). Approximately 21% of the patients who had achieved a therapeutic response at week 12 had not done so at week 8, confirming the longer time to response in depressions with high chronicity. Patients treated with sertraline reported significantly fewer adverse events and were significantly less likely to discontinue treatment due to side effects than imipramine-treated patients

(6.3% vs. 12.0%). ***Conclusion:*** These results indicate that patients suffering from depression with high chronicity can achieve a good therapeutic response to acute treatment with either sertraline or imipramine, although sertraline is better tolerated.

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The Treatment of Chronic Depression, Part 3: Psychosocial Functioning Before and After Treatment With Sertraline or Imipramine

Miller IW, Keitner GI, Schatzberg AF, et al.

Background: Previous research has suggested that depressed patients, and particularly chronically depressed patients, have significant impairments in many areas of their lives. While previous studies suggested that these "psychosocial" impairments improve following pharmacologic treatment, no large scale definitive study using multiple measures of psychosocial functioning has been reported. ***Method:*** We assessed multiple domains of psychosocial functioning using interviewer-rated and self-report measures within the context of a 12-week acute treatment trial of sertraline and imipramine for patients with chronic depression (double depression and chronic major depression). We also compared the psychosocial functioning data of this sample before and after treatment with normative data available from published community samples. ***Results:*** Chronically depressed patients manifested severe impairments in psychosocial functioning at baseline. After treatment with sertraline or imipramine, psychosocial functioning improved significantly. Significant improvements appeared relatively early in treatment (week 4). Despite these highly significant improvements in functioning during acute treatment, the study sample as a whole did not achieve levels of psychosocial functioning comparable to a comparator nondepressed community sample. However, patients who reached full symptomatic response (remission) during acute treatment did have levels of psychosocial functioning in most areas at endpoint that approached or equaled those of community samples. ***Conclusion:*** These results indicate that successful antidepressant treatment with sertraline or imipramine can alleviate the severe psychosocial impairments found in chronic depression.

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SSRI Safety in Overdose

Barbey JT, Roose SP.

Background: The morbidity and mortality caused by tricyclic antidepressant (TCA) overdose are well recognized. Among newer antidepressants, the selective serotonin reuptake inhibitors (SSRIs) are thought to be safer in overdose. This study was designed to describe the signs, symptoms, and mortality associated with SSRI overdose. ***Method:*** English-language articles identified through MEDLINE (1985 through 1997), and case reports from the American Association of Poison Control Centers (AAPCC) (1987 through 1996) and United States Food and Drug Administration (FDA) adverse event database (through 1997) that describe findings of fatal and nonfatal overdoses involving SSRIs alone or in combination with other ingestants were reviewed. ***Results:*** SSRI antidepressants are rarely fatal in overdose when taken alone. During the 10 years that SSRI antidepressants have been marketed, there have been remarkably few fatal overdoses reported in the literature or to the AAPCC or FDA involving ingestion only of an SSRI. Moderate overdoses (up to 30 times the common daily dose) are associated with minor or no symptoms, while ingestions of greater amounts typically result in drowsiness, tremor, nausea, and vomiting. At very high doses (> 75 times the common daily dose), more serious adverse events, including seizures, electrocardiogram (ECG) changes, and decreased consciousness may occur. SSRI overdoses in combination with alcohol or other drugs are associated with increased toxicity, and almost all fatalities involving SSRIs have involved coingestion of other substances. ***Conclusion:*** The SSRI antidepressants are far safer than the TCAs in overdose. There is no apparent difference among SSRIs with respect to overdose safety.

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